REMARKS

I. Introductory Comments

Applicants respectfully request reconsideration of this application in view of the foregoing amendments and following remarks.

After entry of the foregoing amendments, claims 2-3, 5, 9 and 23-37 will be pending in the application. Claims 9, 23-24, 26, 28-29, 31 and 34-36 are currently being amended. No claims are being added. Claim 4 is being canceled.

II. The Sequence Disclosures Comply with 37 C.F.R. §§ 1.821 – 1.825

The Office objected to the application for allegedly failing to comply with the sequence requirements of 37 C.F.R. §§ 1.821 – 1.825.

The Examiner withdrew this rejection following an interview on July 2, 2003. Applicants thank Examiner Canella for the courtesy of that interview, during which the Examiner and J. Huleatt agreed that the application complies with all rules for nucleotide and/or amino acid sequences.

III. Claim 4 is a Proper Dependent Claim

The Office objected to claim 4 as allegedly being of improper dependent form, for failing to further limit the subject matter of a previous claim.

Without acquiescing to the propriety of this objection, Applicants have canceled claim 4. Thus, the objection is now moot.

IV. The Spelling Error in Claim 36 has been Corrected

The Office objected to claim 36 for a misspelling of "hemagglutinin."

Applicants have corrected the spelling error, and request withdrawal of the rejection.

V. Claims 9, 25-26, 28 and 35-36 Comply with the Definite Claiming Requirement of 35 U.S.C. § 112, Second Paragraph

Claims 9, 25-26, 28 and 35-36 were variously rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly

claim the invention. Without acquiescing to the propriety of the rejections, Applicants have amended the claims such that the rejections are moot. Each rejection is addressed separately below.

Claim 9 was rejected for reciting "a second polypeptide" without there being "a first polypeptide." Claim 9 is now amended to recite that the polypeptide according to claim 2, claim 23 or claim 24 is fused to an additional polypeptide, rather than to "a second polypeptide." This clarifying amendment should obviate the rejection.

Claim 26 was rejected because the recitation "nucleic acid molecule further encodes a GST fusion protein" allegedly was not clear. The Office indicated that it was not certain whether the nucleic acid encodes a non-GST heterologous protein as part of the fusion protein. As amended, claim 26 simply recites that the nucleic acid molecule further encodes GST. Support for the amendment exists in the first paragraph on page 15 of the specification.

Claim 28 was rejected as allegedly reciting "an intended use [that] does not influence the limitations of the claim." The Office also stated that it was unclear if "the secretion and/or processing of heterologous proteins encoded therefrom" were part of the claim limitations. As the Examiner suggested, Applicants have deleted the second paragraph from claim 28, such that it simply recites the nucleic acid structure.

Claim 35 was rejected because it allegedly was not clear whether the truncation limitation applies to the dominant negative polypeptides as well as the signaling incompetent polypeptides. Amended claim 35 does not contain any potential ambiguity in this regard, as it recites that "(a) the cytoplasmic domain of said polypeptide is truncated and (b) relative to wild type ALK-7, said polypeptide is signaling incompetent and/or (b) dominant negative." Support for the amendment to claim 35 exists in the paragraph that bridges pages 95-96 of the specification.

Claim 35 was further rejected because the terms "signaling incompetent" and "dominant negative" allegedly were indefinite without reference to a standard polypeptide. Applicants submit that the claim implicitly referenced wild-type ALK-7 as the standard

polypeptide. Nonetheless, they have amended claim 35 to make explicit what previously was implicit.

Claim 36 was rejected because the Office stated that it was unclear whether the HA tag was inserted between residues 230 and 231, or appended to a polypeptide consisting of residues 1-230 of SEQ ID NO:2. Applicants have amended claim 36 to clarify that the polypeptide is truncated at position 230 and characterized by the addition of the HA tag on that same amino acid residue.

The amendments to claims 9, 26, 28 and 35-36 merely clarify the claims, and therefore do not introduce new matter. The amendments also obviate all of the rejections under 35 U.S.C. § 112, second paragraph. Applicants therefore request withdrawal of the rejections.

VI. Enablement of Claims 29 and 34

The Office rejected claims 29 and 34 because the specification allegedly does not provide enablement for all of the recited vectors. Although the Examiner acknowledged that the specification is enabling for the vectors pBR322, pUC118, pUC119, Col E1, pSC101, pACTC184, pVX, pC194, pC221, pT127, p1J101, BPV, vaccinia, 2-micron circle, lambda-gt10, lambda-gt11, pMAM-neo and pRK6, she stated that fC31, pAdRSVOES and pKRC do not appear to be publicly available.

Applicants have deleted reference to vectors fC31, pAdRSVOES and pKRC from claims 29 and 34, thereby obviating the rejection. Applicants reserve the right, however, to pursue claims directed to these vectors at a later time in either this or a continuing application.

VII. Claims 5, 9, 31 and 33-34 Comply with the Enablement Requirement of 35 U.S.C. § 112, First Paragraph

Claims 5, 9, 31 and 33-34 were rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly "does not reasonably provide enablement for vectors and host cells comprised within a transgenic animal or an animal or human being having been treated by gene therapy." The Examiner acknowledged, however, that the application enables

the production and use of isolated vectors and isolated host cells comprising the vectors. Applicants respectfully traverse the rejection.

Claims 5, 31 and 33-34 are drawn to an "isolated, enriched or purified nucleic acid molecule," and amended claim 9 is drawn to a "cultured recombinant cell." Whether the application enables use of this subject matter for gene therapy or transgenic animal production is not relevant to patentability for several reasons.

First, the claims are not limited to gene therapy or transgenic animal uses. The Office correctly noted that the specification "contemplates the use of the instant polynucleotides for the production of transgenic animals (pages 69-71) and in gene therapy (pages 71-76)," but appears improperly to be limiting the claims to these uses. While it is always proper to "read[] a claim in light of the specification, to thereby interpret limitations explicitly recited in the claim," it is impermissible to "read limitations of the specification into a claim." *In re Prater*, 415 F.2d 1393, 1404-05(CCPA 1969). This is exactly what the Office has done.

Second, an applicant need only assert one credible specific utility for a claimed invention to satisfy 35 U.S.C. §§ 101 and 112. Additional statements of utility, even if incredible, do not render the claimed invention lacking in utility. See, *e.g.*, *Raytheon v. Roper*, 724 F.2d 951, 958 (Fed. Cir. 1983, *cert. denied*, 469 U.S. 835 (1984) ("When a properly claimed invention meets at least one stated objective, utility under 3 U.S.C. 101 is clearly shown."); *In re Gottlieb*, 328 F.2d 1016, 1019 (CCPA 1964) ("Having found that the antibiotic is useful for some purpose, it becomes unnecessary to decide whether it is in fact useful for other purposes 'indicated' in the specification as possibly useful.")

Applicants have established that the claimed invention has several credible, substantial utilities related to the biological functions of ALK-7. The sequence of the ALK-7 serine-threonine receptor kinase is extensively characterized, and its expression patterns have been analyzed (specification, pages 87-92). The specification states that ALK-7 is expressed in many different types of cells (pages 89-92). Further, the human ALK-7 of the present invention is expressed in more restricted areas of the brain, i.e., hippocampus, hypothalamic nuclei, sustantia nigra and pituitary gland. This restricted expression pattern strongly

suggests a role for human ALK-7 in the growth and/or survival of neurons and its relevance in treating diseases such as Parkinson's disease, Huntington's disease and Alzheimer's disease (see, for example, page 31 of the specification).

Further, the biological activity of ALK-7 is related to cell activities that include cell proliferation, metastasis, tumor escape, cell adhesion, transformation and apoptosis (specification, paragraph bridging pages 17-18). Dr. Douglass Clary explained, in his previously submitted declaration, the significance of ALK-7 to signaling pathways that promote carcinogenesis.

In this regard, the specification discusses that inhibitors or modulators of ALK-7 can have therapeutic value in the treatment of proliferative diseases such as cancer (pages 31-32). The claimed nucleic acids and recombinant cells clearly can be employed to make proteins useful in methods of identifying such inhibitors or modulators, as described in the specification at page 59, line 16 – page 61, line 11.

The claimed nucleic acids additionally have utility for making proteins that can be used to generate antibodies with binding affinity for ALK-7 and hybridomas containing such antibodies (specification, p. 53, l. 9 – p. 57, l. 8). Such antibodies are useful for detecting an ALK-7 polypeptide in a sample (specification, p. 57, l. 10 – p. 59, l. 14).

Moreover, the claimed nucleic acids are useful as probes for detecting nucleic acids encoding an ALK-7 polypeptide (specification, p. 13, l. 21 – p. 14, l. 24; p. 34, l. 21 – p. 38. l. 7).

Each of these uses constitutes a substantial "real world" utility within the meaning of § 101 and § 112. Accordingly, Applicants respectfully request withdrawal of the rejection.

VIII. Claims 2-4 Comply with the
Enablement Requirement of 35 U.S.C. § 112, First Paragraph

Claims 2-4 were rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly "does not reasonably provide enablement for an endogenous nucleic acid molecule which is directly isolated, enriched or purified from a mammal or a human." Nonetheless, the Examiner acknowledged that the specification is "enabling for a nucleic acid

molecule which is recombinantly expressed and isolated from a mammalian cell or an amplified PCR product which is synthesized using a human mRNA template." Applicants respectfully traverse the rejection.

The Office based this rejection on the specification's statement that ALK-7 polynucleotides were not detectable by northern analysis in some human tissue sources, so PCR amplification was necessary for detection. The Office therefore concluded that ALK-7 polynucleotides are present only at very small quantities in tissues, which would make it very difficult for one to isolate and use endogenous ALK-7 from those tissues.

Applicants submit that the rationale underlying the rejection is flawed. The mere fact that Applicants were able to PCR amplify ALK-7 nucleic acids from tissues with negative northern blots shows that it is possible to isolate a useful quantity of the endogenous nucleic acids. Additionally, Applicants obtained sufficient quantity of ALK-7 DNA from human neuroblastoma cells to sequence and fully characterize the ALK-7 gene, as described in Example 2 of the specification.

Moreover, it is not necessary that every mammalian tissue express high quantities of ALK-7 mRNA for the rejected claims to be enabled. Page 89 of the specification identifies several particular tissue sources for ALK-7 mRNA, including substantia nigra, anterior pituitary, whole brain, cerebellum and prostate. One skilled in the art could go directly to these sources and obtain endogenous ALK-7 nucleic acids without engaging in undue experimentation.

For these reasons, the rejection is improper and Applicants request its withdrawal.

IX. Claims 23-26, 28 and 35-37 Comply with the Enablement Requirement of 35 U.S.C. § 112, First Paragraph

The Office rejected claims 23-26, 28 and 35-37 under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not provide enablement for nucleic acids that encode ALK-7 proteins lacking various domains. Broadly interpreting the claims, the Office stated that they include nucleic acids minimally encoding a single domain of ALK-7, such as the signal domain, transmembrane domain, catalytic domain and so forth. The Office

alleged, however, that a use for such nucleic acids is not apparent because incomplete fragments would not be useful for detecting metastatic lung cancer. Applicants respectfully traverse the rejection.

The amended claims are directed to nucleic acid molecules that encode, at a minimum, the extracellular or catalytic domain of ALK-7. (Exemplary support for the amendments to claims 23 and 24 in this regard exists in the specification at page 34, lines 3-19 and page 51, line 17 – page 52, line 2.) The extracellular and catalytic domains are the functional domains of ALK-7 primarily responsible for signaling and kinase activity. Nucleic acids encoding one or both of these domains have multiple utilities, though the law requires them to have only one credible utility.

At a minimum, nucleic acids encoding ALK-7 extracellular and catalytic domains are useful as probes for detecting nucleic acids encoding an ALK-7 polypeptide (specification, p. 13, l. 21 – p. 14, l. 24; p. 34, l. 21 – p. 38. l. 7).

The nucleic acids also are useful for making ALK-7 fusion proteins (specification, p. 14, l. 25 – p. 15, l. 4). For example, the nucleic acids could be used to make a polypeptide consisting of the ALK-7 catalytic domain and glutathione S-transferase (GST). Such a polypeptide can be employed in biochemical assays for ALK-7 catalytic activity, which are useful for studying ALK-7 substrate specificity and for identifying substances that can modulate ALK-7 catalytic activity.

The claimed nucleic acids have additional utility for producing ALK-7 polypeptides that, when expressed in a cell, are able to form complexes with the natural binding partner(s) of ALK-7 but unable to transmit any signal further downstream into the cell, *i.e.* would be signaling incompetent and thus would be useful for studying the biological relevance of ALP activity (specification, p. 52, l. 25 – p. 53, l. 7). See, as an example, Millauer *et al.*, Nature, 367: 576 (1994).

Additionally, the claimed nucleic acids have utility for making antibodies with binding affinity for ALK-7 and hybridomas containing such antibodies (specification, p. 53, l.

9 – p. 57, l. 8). Such antibodies are useful for detecting an ALK-7 polypeptide in a sample (specification, p. 57, l. 10 – p. 59, l. 14).

Each of these uses constitutes a substantial "real world" utility within the meaning of § 101 and § 112. Accordingly, Applicants respectfully request withdrawal of the rejection.

X. Claims 9, 23-26, 28 and 35 Comply with the Written Description Requirement of 35 U.S.C. § 112, First Paragraph

Claims 9, 23-26, 28 and 35 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not adequately described in the specification. In this regard, the Office stated that the claims are drawn to polynucleotides comprising a "large genus encompassing any polynucleotide which minimally comprises a fragment of SEQ ID NO:2" but lack any functional limitation that distinguishes members of the genus. Applicants respectfully traverse the rejection.

First, the claims are not drawn to "any polynucleotide which minimally comprises a fragment of SEQ ID NO: 2." The polynucleotides of claims 9, 23-26 and 28 all encode, or complement a nucleic acid that encodes, at least the extracellular or catalytic domain of ALK-7. Amended claim 35 recites that the encoded polypeptide comprises the amino acid sequence set forth in SEQ ID NO:2, except that the cytoplasmic domain is truncated. Thus, it does not read on "the truncation of SEQ ID NO:2 down to a single amino acid residue."

Second, the law does not require Applicants to claim their invention in functional terms; neither do the practicalities of this case require it. The Office merely has speculated that the claimed invention "does not exclude proteins which are unrelated to metastatic lung cancer." It has failed, however, to identify any such protein. Absent concrete evidence to support the rejection, the rejection is improper and should be withdrawn.

Claim 23 further was rejected as being drawn, in part, to a nucleic acid comprising a sequence encoding the amino acid residues 193-483 of SEQ ID NO: 2, when the specification identified residues 193-485 as constituting the catalytic domain. According to the Office, the specification does not provide support for a nucleic acid encoding residues 193-483 of SEQ ID NO: 2.

To advance prosecution, but without acquiescing to the rejection, Applicants have amended claim 23 to recite residues 193-485. Exemplary support for the amendment exists at page 52, lines 1-2 of the specification.

XI. Concluding Comments

The application is now in condition for allowance, and favorable reconsideration thereof is respectfully requested.

If the Examiner believes that an interview would advance prosecution of the application, she is invited to contact the undersigned by telephone.

The Commissioner is hereby authorized to charge any additional fees that may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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